Fig. 1

```
ATGTCCATGA ACTGCTGAGT GGATAAACAG CACGGGATAT CTCTGTCTAA  -96
AGGAATATTA CTACACCAGG AAAAGGACAC ATTCGACAAC AGGAAAGGAG  -46
CCTGTCACAG AAAACCACAG TGTCCTGTGC ATGTGACATT TCGCC        -1

ATG GGA AAC AAC TGT TAC AAC GTG GTG GTC ATT GTG CTG CTG CTA   45
Met Gly Asn Asn Cys Tyr Asn Val Val Val Ile Val Leu Leu Leu

GTG GGC TGT GAG AAG GTG GGA GCC GTG CAG AAC TCC TGT GAT AAC   90
Val Gly Cys Glu Lys Val Gly Ala Val Gln Asn Ser Cys Asp Asn

TGT CAG CCT GGT ACT TTC TGC AGA AAA TAC AAT CCA GTC TGC AAG  135
Cys Gln Pro Gly Thr Phe Cys Arg Lys Tyr Asn Pro Val Cys Lys
                             H4-1BB FI

AGC TGC CCT CCA AGT ACC TTC TCC AGC ATA GGT GGA CAG CCG AAC  180
Ser Cys Pro Pro Ser Thr Phe Ser Ser Ile Gly Gly Gln Pro Asn
                                 H4-1BB FII

TGT AAC ATC TGC AGA GTG TGT GCA GGC TAT TTC AGG TTC AAG AAG  225
Cys Asn Ile Cys Arg Val Cys Ala Gly Tyr Phe Arg Phe Lys Lys

TTT TGC TCC TCT ACC CAC AAC GCG GAG TGT GAG TGC ATT GAA GGA  270
Phe Cys Ser Ser Thr His Asn Ala Glu Cys Glu Cys Ile Glu Gly

TTC CAT TGC TTG GGG CCA CAG TGC ACC AGA TGT GAA AAG GAC TGC  315
Phe His Cys Leu Gly Pro Gln Cys Thr Arg Cys Glu Lys Asp Cys

AGG CCT GGC CAG GAG CTA ACG AAG CAG GGT TGC AAA ACC TGT AGC  360
Arg Pro Gly Gln Glu Leu Thr Lys Gln Gly Cys Lys Thr Cys Ser
                                         H4-1BB RI

TTG GGA ACA TTT AAT GAC CAG AAC GGT ACT GGC GTC TGT CGA CCC  405
Leu Gly Thr Phe Asn Asp Gln Asn Gly Thr Gly Val Cys Arg Pro
            H4-1BB RII

TGG ACG AAC TGC TCT CTA GAC GGA AGG TCT GTG CTT AAG ACC GGG  450
Trp Thr Asn Cys Ser Leu Asp Gly Arg Ser Val Leu Lys Thr Gly

ACC ACG GAG AAG GAC GTG GTG TGT GGA CCC CCT GTG GTG AGC TTC  495
Thr Thr Glu Lys Asp Val Val Cys Gly Pro Pro Val Val Ser Phe

TCT CCC AGT ACC ACC ATT TCT GTG ACT CCA GAG GGA GGA CCA GGA  540
Ser Pro Ser Thr Thr Ile Ser Val Thr Pro Glu Gly Gly Pro Gly

GGG CAC TCC TTG CAG GTC CTT ACC TTG TTC CTG GCG CTG ACA TCG  585
Gly His Ser Leu Gln Val Leu Thr Leu Phe Leu Ala Leu Thr Ser

GCT TTG CTG CTG GCC CTG ATC TTC ATT ACT CTC CTG TTC TCT GTG  630
Ala Leu Leu Leu Ala Leu Ile Phe Ile Thr Leu Leu Phe Ser Val

CTC AAA TGG ATC AGG AAA AAA TTC CCC CAC ATA TTC AAG CAA CCA  675
Leu Lys Trp Ile Arg Lys Lys Phe Pro His Ile Phe Lys Gln Pro

TTT AAG AAG ACC ACT GGA GCA GCT CAA GAG GAA GAT GCT TGT AGC  720
Phe Lys Lys Thr Thr Gly Ala Ala Gln Glu Glu Asp Ala Cys Ser
```

Fig.1 (cont'd)

TGC CGA TGT CCA CAG GAA GAA GAA GGA GGA GGA GGA GGC TAT GAG 765
Cys Arg Cys Pro Gln Glu Glu Glu Gly Gly Gly Gly Gly Tyr Glu

CTG TGA 771
Leu ---

TGTACTATCC TAGGAGATGT GTGGGCCGAA ACCGAGAAGC ACTAGGACCC 821
CACCATCCTG TGGAACAGCA CAAGCAACCC CACCACCCTG TTCTTACACA 871
TCATCCTAGA TGATGTGTGG GCGCGCACCT CATCCAAGTC TCTTCTAACG 921
CTAACATATT TGTCTTTACC TTTTTTAAAT CTTTTTTTAA ATTTAAATTT 971
TATGTGTGTG AGTGTTTTGC CTGCCTGTAT GCACACGTGT GTGTGTGTGT 1021
GTGTGTGACA CTCCTGATGC CTGAGGAGGT CAGAAGACAA AGGGTTGGTT 1071
CCATAAGAAC TGGAGTTATG GATGGCTGTG AGCCGGNNNG ATAGGTCGGG 1121
ACGGAGACCT GTCTTCTTAT TTTAACGTGA CTGTATAATA AAAAAAAAAT 1171
GATATTTCGG GAATTGTAGA GATTGTCCTG ACACCCTTCT AGTTAATGAT 1221
CTAAGAGGAA TTGTTGATAC GTAGTATACT GTATATGTGT ATGTATATGT 1271
ATATGTATAT ATAAGACTCT TTTACTGTCA AAGTCAACCT AGAGTGTCTG 1321
GTTACCAGGT CAATTTTATT GGACATTTTA CGTCACACAC ACACACACAC 1371
ACACACACAC ACGTTTATAC TACGTACTGT TATCGGTATT CTACGTCATA 1421
TAATGGGATA GGGTAAAAGG AAACCAAAGA GTGAGTGATA TTATTGTGGA 1471
GGTGACAGAC TACCCCTTCT GGGTACGTAG GGACAGACCT CCTTCGGACT 1521
GTCTAAAACT CCCCTTAGAA GTCTCGTCAA GTTCCCGGAC GAAGAGGACA 1571
GAGGAGACAC AGTCCGAAAA GTTATTTTTC CGGCAAATCC TTTCCCTGTT 1621
TCGTGACACT CCACCCCTTG TGGACACTTG AGTGTCATCC TTGCGCCGGA 1671
AGGTCAGGTG GTACCCGTCT GTAGGGGCGG GGAGACAGAG CCGCGGGGGA 1721
GCTACGAGAA TCGACTCACA GGGCGCCCCG GGCTTCGCAA ATGAAACTTT 1771
TTTAATCTCA CAAGTTTCGT CCGGGCTCGG CGGACCTATG GCGTCGATCC 1821
TTATTACCTT ATCCTGGCGC CAAGATAAAA CAACCAAAAG CCTTGACTCC 1871
GGTACTAATT CTCCCTGCCG GCCCCCGTAA GCATAACGCG GCGATCTCCA 1921
CTTTAAGAAC CTGGCCGCGT TCTGCCTGGT CTCGCTTTCG TAAACGGTTC 1971
TTACAAAAGT AATTAGTTCT TGCTTTCAGC CTCCAAGCTT CTGCTAGTCT 2021
ATGGCAGCAT CAAGGCTGGT ATTTGCTACG GCTGACCGCT ACGCCGCCGC 2071
AATAAGGGTA CTGGGCGGCC CGTCGAAGGC CCTTTGGTTT CAGAAACCCA 2121
AGGCCCCCCT CATACCAACG TTTCGACTTT GATTCTTGCC GGTACGTGGT 2171
GGTGGGTGCC TTAGCTCTTT CTCGATAGTT AGAC 2205

Fig. 2a

human homologue of mouse 4-1bb
h4-1bb Length 838

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  1   AATCAGCTTT GCTAGTATCA TACCTGTGCC AGATTTCATC ATGGGAAACA
 51   GCTGTTACAA CATAGTAGCC ACTCTGTTGC TGGTCCTCAA CTTTGAGAGG
101   ACAAGATCAT TGCAGGATCC TTGTAGTAAC TGCCCAGCTG GTACATTCTG
151   TGATAATAAC AGGAATCAGA TTTGCAGTCC CTGTCCTCCA AATAGTTTCT
201   CCAGCGCAGG TGGACAAAGG ACCTGTGACA TATGCAGGCA GTGTAAAGGT
251   GTTTTCAGGA CCAGGAAGGA GTGTTCCTCC ACCAGCAATG CAGAGTGTGA
301   CTGCACTCCA GGGTTTCACT GCCTGGGGGC AGGATGCAGC ATGTGTGAAC
351   AGGATTGTAA ACAAGGTCAA GAACTGACAA AAAAAGGTTG TAAAGACTGT
401   TGCTTTGGGA CATTTAACGA TCAGAAACGT GGCATCTGTC GACCCTGGAC
451   AAACTGTTCT TTGGATGGAA AGTCTGTGCT TGTGAATGGG ACGAAGGAGA
501   GGGACGTGGT CTGTGGACCA TCTCCAGCTG ACCTCTCTCC GGGAGCATCC
551   TCTGTGACCC CGCCTGCCCC TGCGAGAGAG CCAGGACACT CTCCGCAGAT
601   CATCTCCTTC TTTCTTGCGC TGACGTCGAC TGCGTTGCTC TTCCTGCTGT
651   TCTTCCTCAC GCTCCGTTTC TCTGTTGTTA AACGGGGCAG AAAGAAACTC
701   CTGTATATAT TCAAACAACC ATTTATGAGA CCAGTACAAA CTACTCAAGA
751   GGAAGATGGC TGTAGCTGCC GATTTCCAGA AGAAGAAGAA GGAGGATGTG
801   AACTGTGAAA TGGAAGTCAA TAGGGCTGTT GGGACTTT
```

Fig. 2b

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  1   MGNSCYNIVA TLLLVLNFER TRSLQDPCSN CPAGTFCDNN RNQICSPCPP
 51   NSFSSAGGQR TCDICRQCKG VFRTRKECSS TSNAECDCTP GFHCLGAGCS
101   MCEQDCKQGQ ELTKKGCKDC CFGTFNDQKR GICRPWTNCS LDGKSVLVNG
151   TKERDVVCGP SPADLSPGAS SVTPPAPARE PGHSPQIISF FLALTSTALL
201   FLLFFLTLRF SVVKRGRKKL LYIFKQPFMR PVQTTQEEDG CSCRFPEEEE
251   GGCEL
```
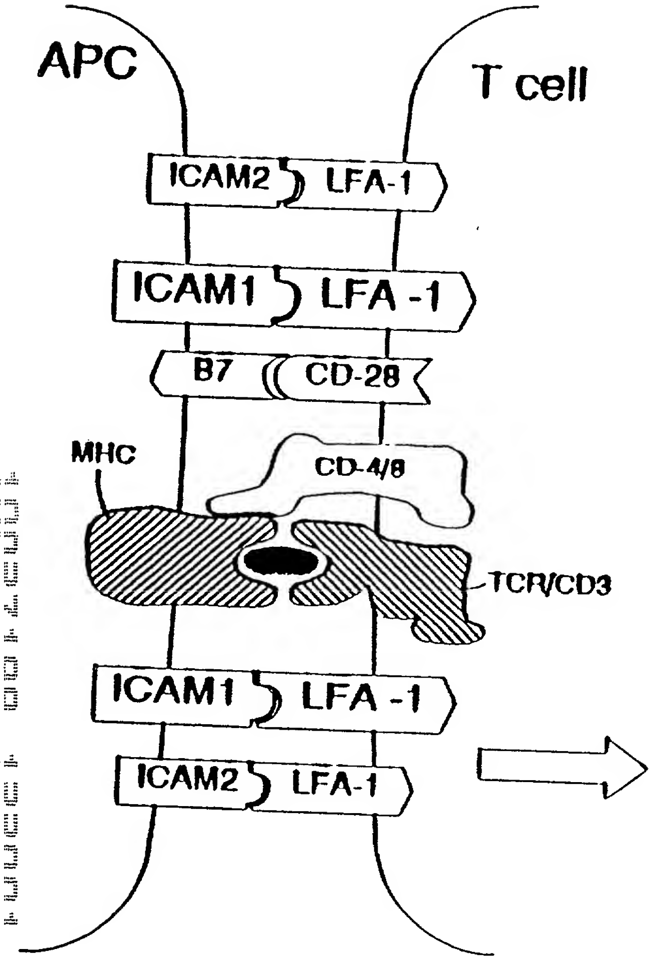
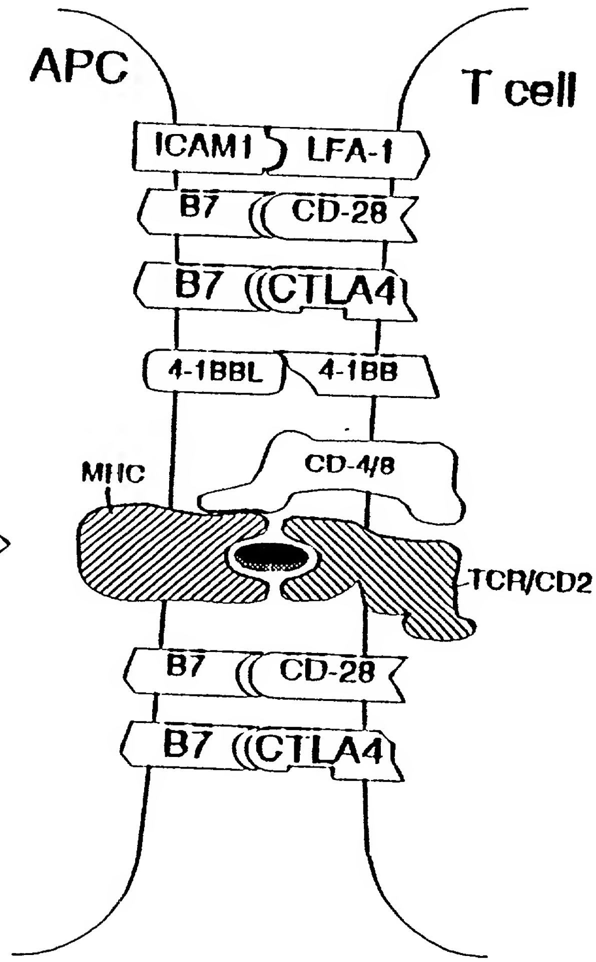



COGNITIVE PHASE
early activation

Fig. 3a



PROLIFERATION
CLONAL EXPANSION
late activation

Fig. 3b

NORMAL T-CELL ACTIVATION PATHWAY

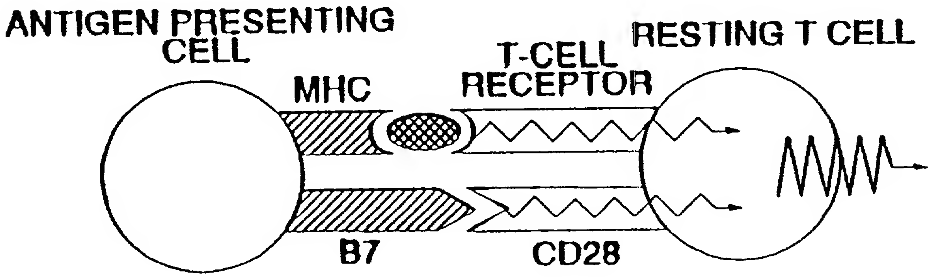


Fig. 4a

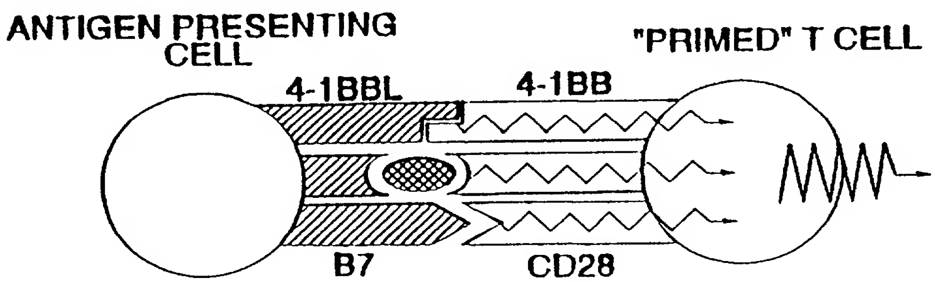


Fig. 4b

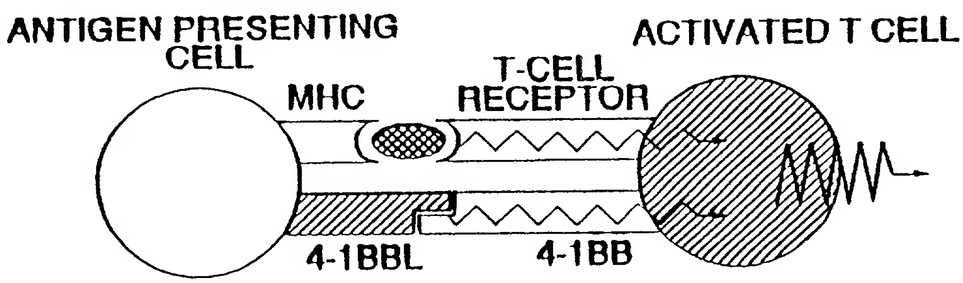


Fig. 4c

BLOCKING STEPS IN T-CELL ACTIVATION PATHWAY

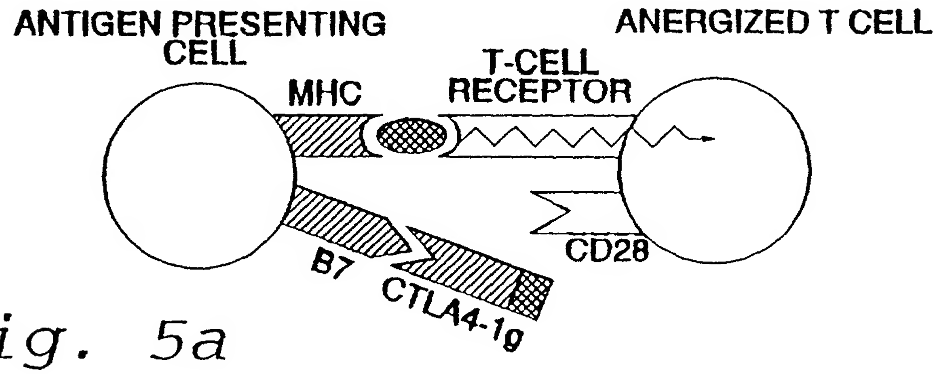


Fig. 5a

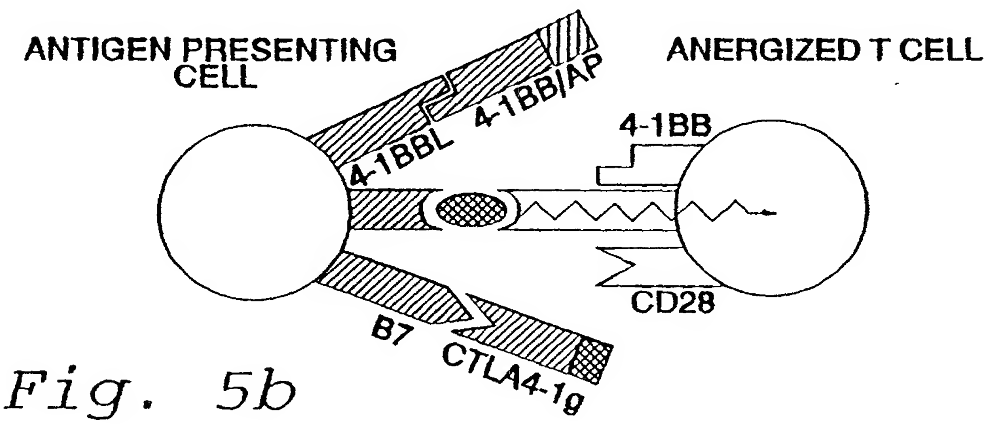


Fig. 5b

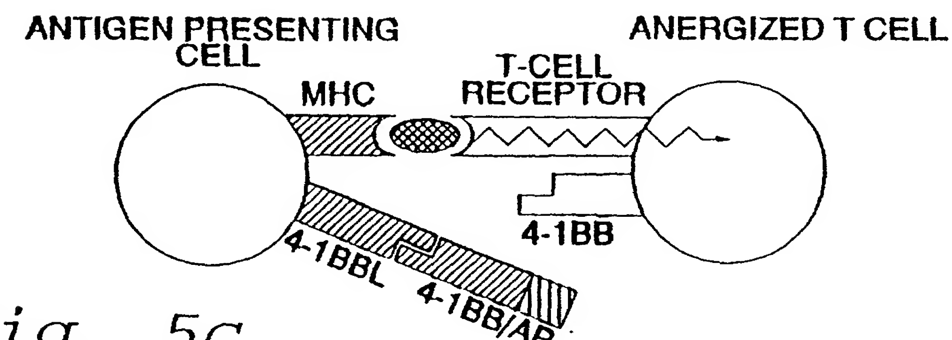


Fig. 5c